



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/171,625	07/02/1999	HUBERT KOSTER	24743-2302US	8272

24961 7590 12/02/2002

HELLER EHRMAN WHITE & MCAULIFFE LLP
4350 LA JOLLA VILLAGE DRIVE
7TH FLOOR
SAN DIEGO, CA 92122-1246

EXAMINER

PONNALURI, PADMASHRI

ART UNIT PAPER NUMBER

1639

DATE MAILED: 12/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/171,625

Applicant(s)
Koster et al

Examiner
Padmeshri Ponnaluri

Art Unit
1639



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Aug 13, 2002
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4 and 11-16 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4 and 11-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 28 6) ☐ Other:

Art Unit: 1639

DETAILED ACTION

NOTE: The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1639.

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.
2. The amendment C, filed on 8/13/02 has been fully considered and entered into the application.
3. Claims 4 and 11-16 are currently pending and are being examined in this application.
4. The new matter rejection of claim 15 set forth in the previous office action mailed on 5/14/02 has been withdrawn in view of applicants response.
5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
6. The scope enablement rejection of claims 4, 11-16 has been maintained for the reasons of record set forth in the previous office action mailed on 5/14/02.

Response to Arguments

7. The rejection of claims 4, 11-16 under 35 U.S.C. 112, first paragraph is maintained for the reasons of record.

Art Unit: 1639

The instant claims briefly recite a process for generating a combinatorial library, by preparing a plurality of immobilized molecules (nucleoside or nucleotide), where in each molecule contains 3 to 10 reactive moieties, each reactive moiety is blocked by a blocking group, and at least three blocking groups on a molecule are independently removable under at least three different conditions; and removing the blocking group and derivitizing the resulting moiety in a preprogrammed, regioselective manner to generate a combinatorial library.

The specification disclosure is based on the use of specific protecting groups and specific reactions and conditions to remove the protecting groups, such that the blocking groups (protecting groups) are activated in regioselective manner. The specification pages 7- 10 disclose the selective orthogonal deprotection . The specification discloses specific protecting groups (reactive in acidic or neutral or basic conditions). The specification discloses that 'selective and orthogonal deprotection are possible if at the linkagesof oligomers, deprotections are selectively done...'. The specification disclosure is based on the use of specific protecting groups at selective positions on the molecules, such that they are regioselectively removed using deprotection reagents.

The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands* (U. S. P. Q. 2d 1400: CAFC 1988) which include: the quantity of experimentation necessary; . the amount of direction or guidance presented; the presence or absence of working examples; . the nature of the invention; the state of the prior art; the predictability of the art; and the breadth of the claims.

Art Unit: 1639

A number of factors would prevent one of ordinary skill in the art from practicing (making and using) the invention without undue experimentation, which are summarized as follows:

- a. The specification fails to give adequate direction and guidance as to the means of making combinatorial libraries using any type of protecting groups to protect any reactive functional groups using deprotection reagents. The specification discloses that the deprotection conditions of one specific protecting group is selected such a way so that the deprotection would not not effect the other protecting groups. The specification discloses that deprotection of npeoc/npe would not effect the trityl ether bond of npe bond. The specification discloses that the deprotection conditions has to be determined so that the conditions would not effect other protecting groups. For example, the specification discloses that 'the stability of R4 during deprotection at 1, 3 and 4 is not necessary, and if R4 is being removed during deprotection at position 4 using reagent IV,... the substitution at position 2 has to be carried out before, and R4 must be stable with reagent II, to guarantee a sequence specific derivitization at position 2. Thus, the use of protecting groups and deprotection reagents are specific, and the sequence of deprotection reactions are specific or predetermined based on the stability of the protecting groups.
- b. The working examples are directed to the use of specific protecting groups and deprotection reagents or conditions.

Art Unit: 1639

c. The breadth of the claims are open-ended regarding the use of protecting groups and deprotection reaction conditions, and the order of the deprotection reactions.

d. The art is inherently unpredictable because the use of protecting groups in a specific position may be unstable during the deprotection conditions, and result in unwanted reactions to occur.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

8. *Applicant's arguments filed on 8/13/02, regarding the scope enablement rejection of claims have been fully considered but they are not persuasive.*

Applicants in response to the scope enablement rejection of claims have been considered. Applicants argue that the specification describes each step of the claimed process. The specification, including the working examples describe in great detail preparation of immobilized oligonucleotides by phosphoramidite method and described modification to the strategy. Applicants in support to this arguments refer to the specification pages 11, 14-20, which specifically teach the use of 'npe', 'npeoc' as protecting groups.

Applicants further argue that 'various blocking groups for the reactive moieties in the molecules on phosphate and nucleoside bases are well characterized in the instant application and are well known to those with skill in the art, as are the deprotecting reagents for selective orthogonal deprotection (see pages 12-13).' Applicants arguments have been considered but are

Art Unit: 1639

not persuasive, since the specification in page 12 discloses that npeoc/npe protection is found to be stable during deprotection conditions. And page 13 of the specification discloses the different protecting groups useful in protecting the phosphate group. The instant claims recite a method in which reactive moieties (3-10) of the molecule are blocked, and at least three of the blocking groups are independently removable under at least three different conditions. Thus, all the reactive moieties are not the phosphate groups as in the applicants arguments. The reactive moieties include bases other than the phosphate groups.

Applicants argue that the level of skill in this art is high, and refer to the numerous articles and patents. Applicants arguments have been considered but are not persuasive, because level of skill in the combinatorial art, but the specification disclosure and several papers which refer to only the use of npe/npeoc protecting groups in multi selective deprotection methods as claimed.

Applicants argue that the at the time of the effective filing date of this application and before, the skilled artisan knew various protecting groups and deprotection reagents and conditions for use in nucleotide/nucleoside synthesis. Applicants arguments have been considered but are not persuasive, because the instant claimed method is not just nucleoside/nucleotide synthesis. The claimed method requires that 'each immobilized molecule (oligonucleotide) contains 3- 10 reactive moieties, each reactive moiety is being blocked by a blocking group, wherein at least three of the blocking groups on each immobilized molecule are independently removable under at least different reaction conditions. Thus, the blocking groups

Art Unit: 1639

have to be stable at various deprotection conditions. The specification disclosure is based on the use of specific blocking groups and does not give guidance for using or selecting any other known blocking groups in the selective deblocking conditions of the claimed method. All the articles applicants referring to are based on the method wherein individual blocking group and one deblocking conditions are used.

The rejections of record have been maintained for the reasons of record.

9. No claims are allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is

Art Unit: 1639

on *Increased Flex Schedule* and can normally be reached on Monday to Friday from 7.00 AM to 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Patent Examiner
Technology Center 1600
Art Unit 1639
02 December 2002


PADMASHRI PONNALURI
PRIMARY EXAMINER